

II. Specification

The amendments to the specification filed on March 20, 2002 were not entered because the number of the amendments allegedly renders it difficult to consider the application, or to arrange the papers for printing or copying. As requested by the office action, a substitute specification excluding the claims has been supplied along with a marked-up copy showing the amendments to be made via the substitute specification relative to the specification at the time the substitute specification is filed. No new matter has been added. As such, applicants respectfully request that the substitute specification be entered and that the objection be withdrawn.

III. Drawings

Figures 3, 4, 5A, and 5B were objected to as allegedly containing new matter. Amended drawings have been submitted to overcome the objections put forth in the office action under the Drawing section in items 1-4. No new matter was entered into the drawings.

Applicants, however, respectfully disagree that the items described in items 5 and 6 of the office action in the drawings section contain new matter. In the originally filed Figure 5B, "Add Hit to Report" was directly connected with "For each Position on Alignment." The Office further alleges that in the newly submitted Figure 5B, the connection between "Set last WasHit=true, Record Start of HitRegion" and "For each Position on Alignment" is new. However, this connection is present in the originally filed figure 5B. There are two differences between the originally filed Figure 5B and the newly filed figure 5B, neither of which is new matter. The first difference is the placement of the boxes on the page. In the new figure 5B the "Set last WasHit=true, Record Start of HitRegion" box has been moved, but its connections have *not* been changed. The other difference is the placement of an arrowhead connecting the "Set last WasHit=true, Record Start of HitRegion" box to the line that continues to the "For each Position on Alignment" box. This is completely a cosmetic change and is not new matter. In view of the foregoing, applicants respectfully request that the new drawings be accepted and the objections to the figures be withdrawn.

IV. The Inventors had possession of the invention at the time of filing

Claims 35-41 and 43-67 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, has possession of the claimed invention. The office action further alleges that

Although the specification describes iron response element and 3' untranslated region of the histone mRNA ..., the specification does not adequately describe that: (1) an oligonucleotide comprising a molecular interaction site that is present in the RNA does not comprise the iron response element in claims 35-41 and 43-51; and (2) an oligonucleotide comprising a molecular interaction site that is present in the RNA does not comprise the iron response element or the 3' untranslated region of the histone mRNA in claims 52-67.

Applicants respectfully disagree.

The standard for determining compliance with the written description requirement of section 112 is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed. See, e.g., *In re Gosteli*, 872 F.2d 1008, 1012, 10 U.S.P.Q.2d 1614, 1618 (Fed. Cir. 1989). Further, it is established law that limitations appearing in claims need not be literally recited in the specification. The issue is not whether words used in the claims are present in the specification but, rather, whether the *concept* expressed by the words is present. *In re Anderson*, 176 U.S.P.Q. 331 (C.C.P.A. 1973).

The specification of the present application thoroughly describes oligonucleotides that comprise a molecular interaction site. The applicants and the Office agree that the specification describes both the iron responsive element and the 3' untranslated region of the histone mRNA. A person of ordinary skill in the art would be able to make and use the invention because the art-skilled would be able to determine if an oligonucleotide contained an iron responsive element or the 3'-untranslated region of the histone mRNA. The sequence of the iron responsive element is well known in the art and is described sufficiently in the specification (see discussion on page 37 of the specification and references cited therein). Additionally, the art-skilled knows where the

3'-untranslated region of the histone mRNA begins. It is well known to a person of ordinary skill in the art that the 3'-untranslated region begins immediately after the stop codon of an mRNA. Thus, all the elements of the claims are present in the application either explicitly or inherently in the description used. Therefore, a person of ordinary skill in the art would have been able to tell that the inventors had complete possession of the claimed invention. As such, applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph be withdrawn.

V. The Claimed Inventions Are Clear and Definite

Claims 50 and 66 stand rejected under 35 U.S.C. § 112, second paragraph for allegedly failing to particularly point out and distinctly claim the subject matter which applicants regards as the invention. Claims 50 and 66 have been amended rendering this rejection moot. Thus, applicants request that the rejections under 35 U.S.C. § 112, second paragraph be withdrawn.

VI. Manzella Reference

Claims 35-40, 43-57, and 59-67 stand rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by or, in the alternative under 35 U.S.C. § 103(a) as allegedly being obvious over Manzella *et al.* (J. Biol. Chem., **267**, 707707082, 1992, hereinafter referred to as the "Manzella reference). Applicants traverse the rejection and respectfully request reconsideration because the Manzella reference does not teach or suggest at least two aspects of applicants' claimed invention.

First, the Manzella reference does not teach or suggest a molecular interaction site that modulates the expression of RNA. The Manzella reference discusses specific protein binding to a conserved region of the ornithine decarboxylase mRNA 5'-untranslated region. As the office action notes, "Manzella *et al.* [does] not directly disclose that modulation of the expression of ornithine decarboxylase mRNA." (Office action, mailed 6/20/2002, p. 8, lines 19-20) The Office alleges that the modulation of the expression is an inherent property of the mRNA. Applicants respectfully disagree. Manzella discloses examples of proteins binding to an

oligonucleotide, but does not disclose that the binding of these proteins to the oligonucleotide that modulates the expression of the mRNA.

Manzella discusses *in vitro* experiments with no expression data shown. It would neither anticipate nor make obvious the claimed invention. It is well known to those of ordinary skill in the art that the binding of a protein to an oligonucleotide may have no impact on its expression. Rather the oligonucleotide could be acting as a scaffold for other proteins or molecules to bind and not impact its expression, but rather could affect the expression of another protein or gene. Therefore, the office action's assertion that the binding of a protein to an oligonucleotide would inherently affect its expression is incorrect.

Second, as acknowledged in the office action mailed June 20, 2002, the molecular interaction site taught by the Manzella reference is not identified in the manner recited in claims 35-40, 43-57, and 59-67. The office action did not consider the identification aspect of applicants' invention as a limitation because it characterized applicants' claims as "product-by-process" claims. Applicants respectfully request reconsideration of this conclusion because applicants' claims are not "product-by-process" claims.

Product-by-process claims are used to describe a product "that resists definition by other than the process by which it is made." *In re Thorpe*, 227 U.S.P.Q. 964, 966 (Fed. Cir. 1985). "That a process limitation appears in a claim does not convert it to a product by process claim." *Fromson v. Advance Offset Plate, Inc.*, 219 U.S.P.Q. 1137, 1141 (Fed. Cir. 1983), see also *Biacore v. Thermo Bioanalysis Corp.*, 79 F. Supp. 2d 422, 456 (D. Del. 1999) (citing *In re Hughes*, 182 U.S.P.Q. 106, 108 (C.C.P.A. 1974); *In re Garnero*, 412 F.2d 276, 279 (C.C.P.A. 1969)) ("The mere use in a claim of structural or characterizing terms derived from processes or methods ... does not prevent a claim from being considered a true product claim"). Applicants have described their claimed invention recited in claims 35-41 and 43-51 primarily in terms of structure or physical characteristics and not by the process by which the invention is made. Therefore, applicants' claims are not true "product-by-process" claims. The process limitation recited in these claims, however, imparts patentability to the claimed compounds.

For at least these reasons, applicants respectfully request that the rejection under 35 U.S.C. § 102(b) and 35 U.S.C. § 103(a) be withdrawn.

VII. The Garcia Reference

Claims 27-29, 35-38, 41, 43-55, and 58-67 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by or, in the alternative under 35 U.S.C. § 103(a) as allegedly obvious over Garcia *et al.* (J. Mol. Biol. **254**, 247-259, 1995, hereinafter referred to as the "Garcia reference") in light of *Molecular Cell Biology* (second edition, edited by Darnell *et al.*, pages 99-101, 1990) and *Textbook of Biochemistry with Clinical Correlations* (third edition, edited by Thomas Devlin, p. 739, 1992). Applicants respectfully disagree.

For a reference to anticipate a claim each and every element as set forth in the claim must be found either expressly or inherently described in a single prior art reference. An anticipation rejection requires a showing that each limitation of a claim be found in a single reference. *Atlas Powder Co. v. E.I. DuPont de Nemours & Co.*, 224 U.S.P.Q. 409, 411 (Fed. Cir. 1984). Because the Garcia reference does not contain all elements of the instant claims, this reference does not anticipate the present application.

The Garcia reference fails to teach or suggest at least two aspects of applicants' claimed invention. First, the Garcia reference fails to teach or suggest an oligonucleotide, let alone an oligonucleotide that comprises a molecular interaction site, as recited in independent claims 27 and 35. Rather, the Garcia reference reports that the ribosome binding domain of *E. coli* translation initiation factor IF3 interacts with 16S RNA. However, the 16S RNA molecule that is relied on for the instant rejection is not an oligonucleotide, as called for by the claims. Applicants' claims clearly distinguish naturally occurring nucleic acid molecules, such as prokaryotic RNA, from oligonucleotides. No oligonucleotide is prepared in, or taught by, the Garcia reference and, thus, the reference does not anticipate the claimed invention.

The Garcia reference further fails to teach or suggest that the molecular interaction site of the 16S RNA is present in "at least one additional prokaryotic RNA," as recited in the claims. The purported molecular interaction site disclosed in the Garcia reference is only disclosed with regard to the 16S RNA molecule, and not with any other RNA.

Finally, with respect to the alternative § 103(a) rejection, the office action fails to make out a *prima facie* showing of obviousness. In establishing a *prima facie* case of obviousness under 35 U.S.C. § 103, it is incumbent upon the Examiner to provide a reason why one of ordinary skill in the art would have been led to modify a prior art reference or to combine reference teachings to arrive at the claimed invention. *Ex parte Clapp*, 227 U.S.P.Q. 972 (Bd. Pat. App. Int. 1985). To this end, the requisite motivation must stem from some teaching, suggestion or inference in the prior art as a whole or from the knowledge generally available to one of ordinary skill in the art and not from appellants' disclosure. See, for example, *Uniroyal Inc. v. Rudkin-Wiley Corp.*, 5 U.S.P.Q.2d 1434 (Fed. Cir. 1988); and *Ex parte Nesbit*, 25 U.S.P.Q.2d 1817, 1819 (Bd. Pat. App. Int. 1992). Here, the office action fails to provide a reason as to why one of ordinary skill in the art would have been led to modify the ribosomal subunit of the Garcia reference to arrive at the oligonucleotide of any claimed invention. Nor does the office action point to any reference that discloses the purported molecular interaction site of the ribosomal subunit is found in an additional prokaryotic RNA. Absent such teachings, the rejection of the claims as allegedly being obvious should be withdrawn.

The office action alleges that the it “*did not need* to ‘provide a reason as to why one of ordinary skill in the art would have been led to modify the ribosomal subunit of the Garcia reference to arrive at the oligonucleotide of claimed invention [.]’ since Garcia *et al.*, in light of the textbook of Molecular Cell Biology and Textbook of Biochemistry with clinical correlations taught [the] claimed invention.” (Emphasis added. Office action mailed 6/20/02, p. 12, lines 1-5).

Applicants respectfully reminds the Office of the Court's view on obviousness

To establish a *prima facie* case of obviousness, “there must be some teaching, suggestion or motivation in the prior art to make the specific combination that was made by the applicant.” *In re Dance*, 48 U.S.P.Q.2d 1635, 1637 (Fed. Cir. 1998). “In other words, *the examiner must show reasons* that the skilled artisan, confronted with the same problem as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed.” *In re Rouffet*, 47 U.S.P.Q.2d 1453, 1458 (Fed. Cir. 1998). (Emphasis Added)

DOCKET NO.: IBIS-0012

PATENT

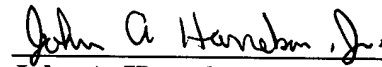
As admitted in the Office Action, no such reasons have been provided in the office action.

For at least these reasons, applicants respectfully request that the rejection under 35 U.S.C. § 102(b) and 35 U.S.C. § 103(a) be withdrawn.

Applicants respectfully submit that the claims are in condition for allowance. An early notice of the same is earnestly solicited.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned **"VERSION WITH MARKINGS TO SHOW CHANGES MADE."**

Respectfully submitted,



John A. Harrelson, Jr.

Registration No. 42,637

Date: October 17, 2002

WOODCOCK WASHBURN LLP
One Liberty Place - 46th Floor
Philadelphia, PA 19103
Telephone: (215) 568-3100
Facsimile: (215) 568-3439

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Substitute specification with markings is attached.

In the Claims:

Please amend claim 50 as follows:

50. (Amended Once) The oligonucleotide of claim 38 wherein said further [other] nucleic acids having secondary structures corresponding to said descriptor elements are identified by searching at least one database, performing clustering and analysis, searching for orthologs, or a combination thereof.

Please amend claim 66 as follows:

66. (Amended Once) The oligonucleotide of claim 55 wherein said further [other] nucleic acids having secondary structures corresponding to said descriptor elements are identified by searching at least one database, performing clustering analysis, searching for orthologs, or a combination thereof.